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EXAMINER
SHUKLA, RAM R

ART UNIT	PAPER NUMBER
1632	11

DATE MAILED: 11/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/762,249	Applicant(s) AMSON ET AL.	
	Examin r Ram R. Shukla	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9-12-02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☐ Claim(s) *26-205* is/are pending in the application.

4a) Of the above claim(s) *26-169 and 178-205* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *170-177* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of the invention of group 13, drawn to an isolated DNA encoding TSAP 21, disclosed in SEQ ID NO 13, a vector comprising the DNA and a host cell transformed with the vector in Paper No. 10 is acknowledged. The traversal is on the ground(s) that all the TSAP and TSIP genes share the same technical feature because they are expressed by the same mechanisms. This is not found persuasive because the mechanism by which they are expressed is not a technical feature of the products or does not tell any thing about the structure of the products, rather it only tells how they are produced. Therefore, the DNA encoding TSAP or TSIP do not share the same technical feature. Next, applicants discuss the example of relationship of DNA to protein (MPEP page AI-60). In response, it is noted that the cited example is not relevant here since claim 178 (for example) does not recite a protein encoded by SEQ ID NO 13. It is noted that claim 178 recites any TSAP 21 protein obtained from cultured host cell transformed with a vector comprising the DNA of SEQ ID NO 13 and therefore, will encompass any TSAP 21 protein present in the cultured host cell.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-25 have been cancelled.

3. New claims 26-205 have been entered.

4. Claims 26-169 and 178-205 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

5. Claims 170-177 drawn to an isolated DNA encoding TSAP 21, disclosed in SEQ ID NO 13, a vector comprising the DNA and a host cell transformed with the vector are under consideration.

Priority

6. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in France on May 8, 1998. It is noted, however, that applicant has not filed a certified copy of the France 98/10077 application as required by 35 U.S.C. 119(b).

Specification

The specification is objected to because it is not arranged in proper sections.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

7. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

8. Claim 170 is objected to because of the following informalities:

Claim 170 is objected because it does not use proper punctuation marks. For example, a comma is missing between TSAP 21 and said in line 1 and between SEQ ID NO 13 and wherein in line 2. Appropriate correction is required.

Double Patenting

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

11. Applicant is advised that should claim 170 be found allowable, claims 171 and 172 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording,

it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

It is noted that claim 171 is drawn to a DNA molecule consisting of the nucleotide sequence of SEQ ID NO 13. Claims 172 and 173 while are dependent on claim 170 and recite new limitations, these limitations do not further limit the invention of claim 171 since these limitations only describe as to how the DNA of claim 170 has been produced or how its expression is induced. It is emphasized that the structure of the DNA of SEQ ID NO 13 will remain the same, irrespective of the method of its production or how and where its expression is induced or activated. Therefore, claims 171 and 172 do not further limit the invention of claim 170.

Claim Rejections - 35 USC § 101

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 170-177 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

In the instant case, claimed invention is drawn to an isolated DNA, wherein the DNA encodes TSAP 21 protein and wherein the DNA consists of the sequence of SEQ ID NO 13. It is noted that claims recite that the claimed DNA is induced during apoptosis or is induced when apoptosis or tumor suppression is induced by p53 or p21. The specification discloses therapeutic and diagnostic uses as the utility for the claimed DNA. However, the specification does not provided any evidence that TSAP 21 is associated with any disease. Furthermore, the specification does not teach any function for the claimed protein. The specification discloses that the expression of TSAP 21 is differentially expressed in cells that express p21 or p53 (see tables 1 and 2). These tables also disclose the size of the mRNA. Table 2 further lists that TSAP has sequence homology to SNARE Syntaxin 11. However, the specification does not provide any guidance as to what is the level of sequence homology between Syntaxin 11 and TSAP 21 proteins. In fact, the specification does not disclose what is the amino acid sequence for the TSAP 21 protein or the protein encoded by SEQ ID NO 13. Furthermore, the specification does not provide any guidance as to what is the function of this protein and there is no evidence of record that TSAP 21 of SEQ ID NO 13 has the function of Syntaxin 11.

The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish any function for the DNA sequence disclosed in SEQ ID NO 13 as shown by structural and functional properties. The recited SEQ ID NO is a cDNA for which no biological function has been established. It is known in the art that the SNARE proteins are a family of protein whose expression varies from tissue to tissue or during development (see Advani et al. Seven novel mammalian SNARE proteins localize to distinct membrane compartments. J of Biological Chemistry 273:10317-10324, 1998), localize to different membrane compartments of a cell and therefore will have very divergent functions (see the abstract). However, the specification fails to show a single working example that establishes that the what is the functions of the protein encoded by the DNA sequence of SEQ ID NO 13 and there is no evidence of record to clearly indicate the relationship of the TSAP 21 protein to SNARE or Syntaxin protein, by substantial sequence homology and/or functional assay of the protein.

It is reiterated that the specification alleges that the instant nucleic acid encodes for Syntaxin related protein based on homology of the deduced amino acid sequences with nucleotides (see table 2). However, no sequence comparisons are taught by specification as filed, nor are any specific similarities to other Syntaxin like proteins disclosed, such as common motifs of conservation, functional motifs etc. When TSAP 21 is compared with Syntaxin 1 DNA, there is sequence identity only in region of 467 nucleotides of TSAP 21 with 535-100 of Syntaxin 1. Since nt 55 to 918 of Syntaxin 1 encode for the protein, it is clear that the structure of TSAP 21 will be significantly different from that of Syntaxin 1. Therefore, the function of Syntaxin 1 cannot be attributed to TSAP 21. In conclusion, the specification fails to teach that polypeptide encoded by SEQ ID NO 13 has the biological activity of a Syntaxin explicitly or implicitly as putatively considered by the specification. In other words, the only immediate apparent utility for the instant invention would be its further scientific characterization as a putative Syntaxin.

In view of the foregoing, one skilled in the art would not readily attribute Syntaxin activity to the protein encoded by the instantly claimed nucleic acid and it is unclear that Syntaxin activity could be attributed to the deduced amino acid sequence of the claimed nucleic acid. Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

14. Claims 170-177 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 170-177 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

As noted above in regard to the utility rejection, claimed invention is drawn to an isolated DNA, wherein the DNA encodes TSAP 21 protein and wherein the DNA consists of the sequence of SEQ ID NO 13. It is noted that claims recite that the claimed DNA is induced during apoptosis or is induced when apoptosis or tumor suppression is induced by p53 or p21. The specification discloses therapeutic and diagnostic uses as the utility for the claimed DNA. However, the specification does not provided any evidence that TSAP 21 is associated with any disease.

Additionally, the specification does not teach any function for the claimed protein. The specification on pages 9-19 discloses that the expression of TSAP 21 (SEQ ID NO 13) is increased in a K562 cell line that is infected with H-1 parvovirus. The results in tables 1-3 disclose several sequences that are overexpressed in these cells. However, the model used in the specification is a cell line and therefore while it may be related to p53 or p21 related gene expression pathway, there is no evidence of record that the expression of TSAP 21 is related to any disease occurring in an animal. It is noted that a diagnostic test is performed in an animal sample derived from an animal that has some disease or condition and in the absence of any relationship of TSAP 21 with any disease in an animal, it is not clear what will be diagnosed using TSAP 21 DNA as a probe.

Roperch et al (Roperch et al. SIAH-1 promotes apoptosis and tumor suppression through a network involving the regulation of protein folding, unfolding, and trafficking: identification of common effectors with p53 and p21Waf1. Proc. Natl. Acad. Sci. USA 96:8070-8073, 1999) reported the cloning of TSAP 21 gene, however, this paper also except for predicting the sequence homology with Syntaxin 1 gene does not provide any description of the function of the TSAP protein. When TSAP 21 is compared with Syntaxin 1 DNA, there is sequence identity only in region of 467 nucleotides of TSAP 21 with 535-100 of Syntaxin 1. Since nt 55 to 918 of Syntaxin 1 encode for the protein, it is clear that the structure of TSAP 21 will be significantly different from that of Syntaxin 1. Therefore, the function of Syntaxin 1 cannot be attributed to TSAP 21. In summary, the specification fails to teach the function of TSAP 21 and also it does not establish relationship of TSAP 21 expression with any disease. It is emphasized that the specification does not disclose what is the amino acid sequence for the TSAP 21 protein or the protein encoded by SEQ ID NO 13. In other words, it is not clear whether SEQ ID NO 13 encodes any protein, what is the ORF in SEQ ID NO 13. Therefore, an artisan would not have known what disease to diagnose using TSAP 21 DNA and therefore would not know how to use the TSAP 21 DNA or vector comprising the DNA or the host cell comprising the vector. An artisan would have to carry out extensive experimentation to first study, what protein is encoded by SEQ

ID NO 13, the function of TSAP 21, study its relationship to a disease and such experimentation will be undue because neither the specification nor the art of record teaches as to what experiments to perform and how.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 170-177 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 170 is indefinite because it is unclear as to how the wherein clause reciting "wherein the expression of said TSAP 21 is induced during apoptosis or tumor suppression" further limits the claimed invention since the wherein clause indicates when the DNA is produced. However, this is not a characteristic of the DNA that will define the structure or function of the claimed DNA.

Claim 172 is indefinite because it is unclear as to how the wherein clause reciting "wherein the expression of said TSAP 21 is activated by ..... transfectants" further limits the claimed invention since the wherein clause indicates when the DNA is produced. However, this is not a characteristic of the DNA that will define the structure or function of the claimed DNA.

Claim 171 is indefinite because it is unclear as to how the wherein clause reciting "wherein said apoptosis or tumor suppression is induced by p53 or p21" further limits the claimed invention since the wherein clause indicates when the DNA is produced. However, this is not a characteristic of the DNA that will define the structure or function of the claimed DNA.

Claim 175 recites the limitation "said virus" in line 1. There is insufficient antecedent basis for this limitation in the claim since neither claims 174 nor claim 175 recites the term "a virus".

Claim 176 is vague and indefinite since it is unclear as to what is meant by the term "a naked nucleic acid vector". The specification does not define as to what will be considered a naked nucleic acid vector.

19. No claim is allowed.

20. The DNA sequence of SEQ ID NO 13 is free of the prior art of record.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Tiffiany N. Tabb whose telephone number is (703) 605-1238.

Ram R. Shukla, Ph.D.

RAM R. SHUKLA, PH.D
PATENT EXAMINER